

APPLICANT'S REMARKS

1. Status of the Claims

Claims 1–14, 19, and 20 are pending. Claims 1 and 20 are currently amended. Claims 15–18 are canceled.

Claim 20 was newly presented in the last Amendment dated June 3, 2009. However, the Examiner does not address claim 20 in the present Office Action. The Applicant respectfully requests clarification of this discrepancy on the record.

2. Claims 1–6, 8, 11, 13, 14, 17, and 19 Rejected Under 35 U.S.C. 103(a) Based on DOMINGUES in view of WYLLIE

Claims 1–6, 8, 11, 13, 14, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over DOMINGUES in view of WYLLIE.

For determining obviousness, all words in a claim must be considered in judging the patentability of that claim against the prior art (*In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)). The inherent teaching of a prior art reference arises both in the context of anticipation and obviousness. (see *In re Grasselli*, 713 F.2d 731, 739 (Fed.Cir.1983)) “In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly

inherent characteristic necessarily flows from the teachings of the applied prior art." (Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original))

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. (In re Rijckaert, 9 F.3d 1531, 1534 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art))

The Examiner asserts that DOMINGUES teaches the steps of the presently claimed methods, except for steps (e) and (f), which steps the Examiner argues are taught by WYLLIE. The Examiner concludes that one skilled in the art would be motivated to combine DOMINGUES and WYLLIE with a reasonable expectation of success because WYLLIE teaches that human IL-4 is predicted to have high affinity to the immobilized metal during IMAC.

The Examiner further asserts that the purity of IL-4 or mutants thereof purified using Zn-chelating affinity chromatography would necessarily have a purity of about 90% as estimated by SDS-PAGE analysis.

The Applicant respectfully disagrees with the Examiner and submits that claims are not obvious based on DOMINGUES and WYLLIE. In particular, the presently claimed purity and recovery are not inherently disclosed by the cited references.

As acknowledged by the Examiner, DOMINGUES is silent regarding IMAC. Therefore, the allegedly inherent characteristics cannot necessarily flow from the teachings of DOMINGUES.

Turning to WYLLIE, IL-4 is quantitatively recovered (>85%) in the elute when located onto zinc-chelating Sepharose at pH 7.0, 7.2, or 7.5 and above. WYLLIE does not provide any purity data regarding IL-4. However, WYLLIE does provide purity data for IL-13. When a relatively pure preparation of IL-13 (>80%) was applied to the resin at pH 7.5 and eluted with imidazole gradient, recovery was 30% (similar to pH 7.2 separation), but the purity was >90%. Thus, since the only example in WYLLIE with purity data actually teaches low recovery with high purity, the Applicants respectfully submit that WYLLIE does not teach that IMAC inevitably provides high recovery and high purity of IL-4.

In light of the foregoing, the Applicant respectfully submits that the Examiner has not explained how WYLLIE's disclosure necessarily or inevitably provides the presently claimed high recovery and high purity of denatured IL-4.

Therefore, the Applicant respectfully submits that, even assuming *arguendo* that DOMINGUES and WYLLIE may be properly combined, the resulting combinations do not disclose or even suggest all the features recited in the present claims.

The Applicant respectfully requests that the §103(a) rejection of claims 1–6, 8, 11, 13, 14, 17, and 19 be reconsidered and withdrawn.

3. Claims 7, 9, 10, 12, 15 and 16 Rejected Under 35 U.S.C. 102(e) Based on DOMINGUES in view of WYLLIE and further in view of APELER, GELLMAN, BONSCH, or THØGERSEN

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over DOMINGUES in view of WYLLIE and further in view of APELER. The Office Action states that APELER teaches the expression of the particular human interleukin-4 mutant, R121D Y124D, that is claimed.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over DOMINGUES in view of WYLLIE and further in view of GELLMAN. The Office Action states that GELLMAN teaches the use of an artificial chaperone, such as beta-cyclodextrin.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over DOMINGUES in view of WYLLIE and further in view of BONSCH. The Office Action states that BONSCH teaches the expression of the particular murine homolog of human interleukin-4 that is claimed, Q116D and Y119D.

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over DOMINGUES in view of WYLLIE and further in view of THØGERSEN. The Office Action states that it would have been obvious to carry out the claimed method with the refolding step being performed while the IL-4 remains bound to the IMAC system in view of the

teachings in THØGERSEN pertaining to the use of matrix-assisted folding of various polypeptides.

For the reasons stated above, the Applicant respectfully submits that the combination of DOMINGUES and WYLLIE does not disclose or even suggest the presently claimed recovery and purity. Combining DOMINGUES and WYLLIE with APELER, GELLMAN, BONSCH, or THØGERSEN does not cure this deficiency because APELER, GELLMAN, BONSCH, and THØGERSEN are silent regarding IMAC.

Therefore, the Applicant respectfully submits that, even assuming *arguendo* that the references may be properly combined, the resulting combinations do not disclose or even suggest all the features recited in the present claims.

In light of the foregoing, the Applicants respectfully request that the §103(a) rejection of claims 7, 9, 10, 12, 15 and 16 be reconsidered and withdrawn.

4. Conclusion

Favorable reconsideration of this application is respectfully requested.

Respectfully submitted,

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